alkaline phosphatase complementary DNA (Keun, *et al.*, *Proc. Natl. Acad. Sci. USA 82*:8715-8719 (1985)).

Amendments to the specification are indicated in the attached "Marked Up Version of Amendments" (pages i-ii).

REMARKS

Specification Amendments

The Specification is amended to add low, medium and high stringency conditions. Support for this amendment is found, for example, in the Specification (at page 26, lines 25-28), which states "See, e.g., Ausubel *et al.*, eds. *Current Protocols in Molecular Biology*, Wiley Interscience, N.Y. (1987, 1992, 1993), and Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press (1989), the entire contents of which are incorporated herein by reference" and in Ausubel *et al.*, *supra*, at 2.10.2-2.10.3. The relevant portions of Ausubel *et al.* and Sambrook *et al.* are attached hereto as Exhibits A and B, respectively. No new matter has been added.

Rejection of Disclosure

According to the Examiner, the instant specification, which claims priority to US Application No. 09/133,119, now U.S. Patent No. 6,277,969, as a continuation, differs from the '119 specification at page 29, line 26, which has deleted the definitions for low, medium and high stringency that are present in the '119 application. Thus, the Examiner states that the instant application is a continuation-in-part of the '119 application rather than a continuation.

Applicants respectfully disagree. The '119 application, as originally filed, did not contain the definitions for low, medium and high stringency. These definitions were added to the specification in an Amendment that was filed with the United States Patent and Trademark Office (USPTO) on March 22, 2000, in response to an Office Action mailed from the USPTO on September 22, 1999. The Patent Office entered the amendment into the record. Therefore, the disclosure of the instant application, as originally filed, is substantially the same as that of the parent '119 application as originally filed. Thus, the instant application is properly designated as

a continuation of the '119 application. Reconsideration and withdrawal of the objection are respectfully requested.

The Examiner also objected to the specification for failing to provide proper antecedent basis for the claimed subject matter, specifically the phrase "high stringency" is missing from the specification.

Applicants have amended the instant specification to include and define low, medium and high stringency. Again, this amendment was acceptable to the Patent Office and entered into the record in prior application 09/133,119 (now U.S. Patent No. 6,277,969), which is a parent application to the instant application. Furthermore, such hybridization conditions are well known to those of skill in the art. For example, stringent conditions are described in Sambrook, J. *et al.*, *supra,* at page 11.45 -11.61 ("Conditions for Hybridization of Oligonucleotide Probes") and Ausubel, F.N. *et al., Current Protocols in Molecular Biology*, at Chapter 2 ("Preparation and Analysis of DNA"), Chapter 14 ("In situ Hybridization and Immunochemistry") and Chapter 15 ("The Polymerase Chain Reaction"), Greene Publishing Assoc. and Wiley-Interscience (1989). Relevant portions of Chapter 2 of Ausubel *et al.* are included herein as Exhibit A. Relevant portions of Sambrook are included herein as Exhibit B. Hybridization conditions listed in these references include ionic strength and temperature of the post-hybridization wash. See, for example, Exhibit A at 2.10.2-3 and 2.10.10-11 and Exhibit B at 11.45. One skilled in the art would be able to optimize hybridization conditions by varying the specifically exemplified conditions discussed in the references and Specification. Such optimization is routine in the art.

Reconsideration and withdrawal of the objection are respectfully requested.

Rejection of Claims 7-12 Under 35 U.S.C. §101

Claims 7-12 are rejected under 35 U.S.C. §101 as directed to non-statutory subject matter. According to the Examiner, Claims 7-12 are drawn to expression vectors comprising a nucleic acid sequence and can be construed as reading on an expression vector comprised within a human having undergone treatment comprising the administration of said claimed expression vectors.

Applicants are confused by the Examiner's rejection and clarification is respectfully requested. Claims 7-12 are directed towards expression vectors comprising the nucleic acid molecule according to Claims 1-6, respectively. 35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed expression vectors comprising nucleic acid molecules are a new and useful composition. The claimed expression vectors are a nonnaturally occuring composition of matter and are clearly new and patentable (see MPEP §2105). Additionally, the claimed expression vectors are useful because, as discussed below, the specification discloses many uses for the claimed expression vectors. Furthermore, the instant claims are representative of standard claims presented to, and issued by, the USPTO. For example, see Claims 3 and 4 of U.S. Patent No. 6,277,969, which the Examiner has allowed to issue (a copy of the cover page and claims for 6,277,969 is enclosed as Exhibit C for the Examiner's convenience). See also Claim 13 of U.S. Patent No. 6,573,077; Claim 8 of U.S. Patent No. 6,573,368; Claims 17 and 18 of U.S. Patent No. 6,569,667; and Claim 5 of U.S. Patent No. 6,570,062 (copies of the cover page and claims for the referenced patents are enclosed as Exhibits D-G for the Examiner's convenience).

MPEP §2107.02 states:

> Office personnel should also be especially careful not to read into a claim unclaimed results, limitations or embodiments of an invention. See *Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 20 USPQ2d 1094 (Fed. Cir. 1991); *In re Krimmel*, 292 F.2d 948, 130 USPQ 215 (CCPA 1961). Doing so can inappropriately change the relationship of an asserted utility to the claimed invention and raise issues not relevant to examination of that claim.

The Examiner appears to be reading an unclaimed embodiment into the Claims 7-12. The instant claims are novel composition claims and do not recite methods of delivery for gene therapy. Thus, the Examiner has changed the relationship of an asserted utility to the claimed invention and has raised an issue not relevant to the examination of Claims 7-12.

As Claims 7-12 are directed to patentable subject matter under 35 U.S.C. §101, the amendment suggested by the Examiner need not be addressed. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 7-12 Under 35 U.S.C. §112, First Paragraph

Claims 7-12 are rejected under 35 U.S.C. §112, first paragraph, because, according to the Examiner, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Examiner has rejected "the claims on the grounds that the claims are clearly intended to encompass methods of gene therapy." However, according to the Examiner, the specification is not enabling for gene therapy.

Again, Applicants are confused and further clarification of this rejection is respectfully requested. The claims are not drawn to or limited by any recited method or use. Claims 7-12 are directed towards expression vectors comprising the nucleic acid molecule according to Claims 1-6, respectively. The specification provides ample teachings to enable one of skill in the art to clone an isolated nucleic acid molecule according to Claims 1-6 into an expression vector (see Detailed Description at page 44, lines 17 to 25).

MPEP 2164.01(c) states:

> when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use.

The specification enables many uses for the claimed expression vectors. For example, on page 30, line 5 to page 31, line 2, the specification describes that a polynucleotide encoding an anti-TNF variable or constant region can be cloned into an expression vector which is capable of expressing a protein which competitively inhibits the binding of an anti-TNF antibody, such as A2 or cA2. The instant claims are representative of standard claims presented to, and issued by, the USPTO. Moreover, instant Claims 7-12 are directed to expression vectors with a similar scope of coverage as Claims 3 and 4 of the parent application U.S. Patent No. 6,277,969, which the Examiner found to be enabled by the same specification. Therefore the instant specification

enables one skilled in the art to make and use the invention commensurate in scope with Claims 7-12. Reconsideration and withdrawal of the rejection are respectfully requested.

Information Disclosure Statement

A Supplemental Information Disclosure Statement (SIDS) is being filed concurrently herewith. Applicants thank the Examiner for the telephone interview on July 10, 2003, regarding the references cited in the SIDS. As discussed in the interview, Applicants will provide copies of the references in the instant application and then will disclose the references, without providing copies, in the currently pending daughter applications. Entry of the IDS is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTS

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Replace the paragraph at page 29, line 10 through page 30, line 4 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

A suitable oligonucleotide, or set of oligonucleotides, which is capable of encoding a fragment of the variable or constant anti-TNF region (or which is complementary to such an oligonucleotide, or set of oligonucleotides) is identified (using the above-described procedure), synthesized, and hybridized by means well known in the art, against a DNA or, more preferably, a cDNA preparation derived from cells which are capable of expressing anti-TNF antibodies or variable or constant regions thereof. Single stranded oligonucleotide molecules complementary to the "most probable" variable or constant anti-TNF region peptide coding sequences can be synthesized using procedures which are well known to those of ordinary skill in the art (Belagaje, *et al., J. Biol. Chem. 254*:5765-5780 (1979); Maniatis, *et al., In: Molecular Mechanisms in the Control of Gene Expression,* Nierlich, *et al.*, Eds., Acad. Press, NY (1976); Wu, *et al., Prog. Nucl. Acid Res. Molec. Biol. 21*:101-141 (1978); Khorana, *Science 203*:614-625 (1979)). Additionally, DNA synthesis can be achieved through the use of automated synthesizers. Techniques of nucleic acid hybridization are disclosed by Sambrook *et al. (infra),* and by Haymes, *et al.* (In: *Nucleic Acid Hybridization, A Practical Approach,* IRL Press, Washington, DC (1985)), which references are herein incorporated by reference. Hybridization wash conditions can include wash solution of 0.2x SSC/0.1% SDS and incubation with rotation for 10 minutes at room temperature, (low stringency wash), wash solution of prewarmed (42° C) 0.2x SSC/0.1% SDS and incubation with rotation for 15 minutes at 42° C (medium stringency wash) and wash solution of prewarmed (68° C) 0.1x SSC/0.1% SDS and incubation with rotation for 15 minutes at 68° C (high stringency wash). See Ausubel *et al. (infra)*. Techniques such as, or similar to, those described above have successfully enabled the cloning of genes for human aldehyde dehydrogenases (Hsu, *et al., Proc. Natl. Acad. Sci. USA 82*:3771-3775 (1985)), fibronectin (Suzuki, *et al., Bur. Mol. Biol. Organ. J. 4*:2519-2524 (1985)), the human estrogen receptor gene (Walter, *et al., Proc. Natl. Acad. Sci. USA 82*:7889-7893

(1985)), tissue-type plasminogen activator (Pennica, *et al.*, *Nature 301*:214-221 (1983)) and human term placental alkaline phosphatase complementary DNA (Keun, *et al.*, *Proc. Natl. Acad. Sci. USA 82*:8715-8719 (1985)).